Fast Facts on Osteogenesis Imperfecta

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Definition

Osteogenesis imperfecta (OI) is a genetic disorder characterized by bones that break easily, often from little or no apparent cause. There are at least four recognized forms of the disorder, representing a range of severities. For example, a person may have just a few or as many as several hundred fractures in a lifetime.

Prevalence

While the number of people affected with OI in the United States is unknown, the best estimate suggests a minimum of 20,000 and possibly as many as 50,000.

Diagnosis

OI is caused by a genetic defect that affects the body's production of collagen. Collagen is the major protein of the body's connective tissue and can be likened to the framework around which a building is constructed. In OI, a person has either less collagen than normal, or a poorer quality of collagen than normal, leading to weak bones that fracture easily.

It is often, though not always, possible to diagnose OI based solely on clinical features. Clinical geneticists can also perform biochemical (collagen) or molecular (DNA) tests that can help confirm a diagnosis of OI in some situations. These tests generally require several weeks before results are known. Both the collagen biopsy test and DNA test are thought to detect almost 90% of all collagen type 1 mutations.

A positive collagen type 1 study confirms the diagnosis of OI, but a negative result leaves open the possibility that either a collagen type 1 mutation is present but was not detected or the patient has a form of the disorder that is not associated with collagen type 1 mutations. Therefore, a negative collagen type 1 study does not rule out OI.

Clinical Features

The characteristic features of OI vary greatly from person to person, even among people with the same type of OI, and even within the same family, and not all characteristics are evident in each case. The general features of the four recognized types of OI, which vary in characteristics and severity, are as follows:

Type I

- Most common and mildest type of OI.
- Bones predisposed to fracture. Most fractures occur before puberty.
- Normal or near-normal stature.
- Loose joints and muscle weakness.
- Sclera (whites of the eyes) usually have a blue, purple, or gray tint.
- Triangular face.
- Tendency toward spinal curvature.
- Bone deformity absent or minimal.
- Brittle teeth possible.
- Hearing loss possible, often beginning in early 20s or 30s.
- Collagen structure is normal, but the amount is less than normal.

Type II

- Most severe form.
- Frequently lethal at or shortly after birth, often due to respiratory problems. In recent years, some people with Type II have lived into young adulthood.
- Numerous fractures and severe bone deformity.
- Small stature with underdeveloped lungs.
- Collagen improperly formed.

Type III

- Bones fracture easily. Fractures often present at birth, and x rays may reveal healed fractures that occurred before birth.
- Short stature.
- Sclera have a blue, purple, or gray tint.
- Loose joints and poor muscle development in arms and legs.
- Barrel-shaped rib cage.
- Triangular face.

- Spinal curvature.
- Respiratory problems possible.
- Bone deformity, often severe.
- Brittle teeth possible.
- Hearing loss possible.
- Collagen improperly formed.

Type IV

- Between Type I and Type III in severity.
- Bones fracture easily, most before puberty.
- Shorter than average stature.
- Sclera are white or near-white (i.e., normal in color).
- Mild to moderate bone deformity.
- Tendency toward spinal curvature.
- Barrel-shaped rib cage.
- Triangular face.
- Brittle teeth possible.
- Hearing loss possible.
- Collagen improperly formed.

For a number of years, investigators have been doing special studies on the appearance of OI bone under the microscope. They noticed that some people who are clinically within the Type IV group had a distinct pattern to their bone. When they reviewed the full medical history of these individuals, they found that groups had other features in common. They named these groups Types V and VI OI. Patients in these two groups do not have evidence of having mutations in the type I collagen genes.

Type V

- Clinically similar to Type IV.
- A dense band seen on x rays adjacent to the growth plate of the long bones.
- Unusually large calluses, called hypertrophic calluses, at the sites of fractures or surgical procedures. (A callus is an area of new bone that is laid down at the fracture site as part of the healing process.)
- Calcification of the membrane between the radius and ulna (the bones of the forearm). This leads to restriction of forearm rotation.
- White sclera.
- Normal teeth.
- Bone has a “mesh-like” appearance when viewed under the microscope.

Type VI
People with this type of OI are moderately to severely affected. They have normal (white or slightly blue) sclera and the teeth are not affected. The alkaline phosphatase (an enzyme linked to bone-forming cell activity) activity level is slightly elevated in OI Type VI, and this can be determined by a blood test. Because the clinical features are so similar to other moderate forms of OI, a bone biopsy is the only method by which OI Type VI can be diagnosed with certainty. The bone from patients with this form has a distinctive "fish-scale" appearance when viewed under the microscope. Eight people with this type of OI have been identified.

Inheritance Factors

Most cases of OI are caused by a dominant genetic defect. Some children with OI inherit the disorder from a parent. Other children are born with OI even though there is no family history of the disorder. In these children, the genetic defect occurred as a spontaneous mutation.

Because the defect — whether inherited or due to a spontaneous mutation — is usually dominant, a person with OI has a 50 percent chance of passing on the disorder to each of his or her children. Genetic counselors can help people with OI and their family members further understand OI genetics and the possibility of recurrence, and assist in prenatal diagnosis for those who wish to exercise that option. For more information on OI inheritance, see the OI Foundation fact sheet titled "Genetics."

Treatment

There is not yet a cure for OI. Treatment is directed toward preventing or controlling the symptoms, maximizing independent mobility, and developing optimal bone mass and muscle strength. Care of fractures, extensive surgical and dental procedures, and physical therapy are often recommended for people with OI. Use of wheelchairs, braces, and other mobility aids is common, particularly (although not exclusively) among people with more severe types of OI.

A surgical procedure called "rodding" is frequently considered for individuals with OI. This treatment involves inserting metal rods through the length of the long bones to strengthen them and prevent and/or correct deformities. For more information, see the OI Foundation's fact sheet on "Rodding Surgery."

Several medications and other treatments are being explored for their potential use to treat OI. The OI Foundation can provide current information on research studies and experimental treatments for OI, as well as information to help individuals decide whether to participate in clinical trials.

People with OI are encouraged to exercise as much as possible to promote muscle and bone strength, which can help prevent fractures. Swimming and water therapy are common exercise choices for people with OI, as water allows independent movement with little risk of fracture. For those who are able, walking (with or without mobility aids) is excellent exercise. Individuals with OI should consult their physician and/or physical therapist to discuss appropriate and safe exercise.

Children and adults with OI will also benefit from maintaining a healthy weight, eating a nutritious diet, and avoiding activities such as smoking, excessive alcohol and caffeine consumption, and taking steroid medications — all of which may deplete bone and exacerbate bone fragility. For more information on nutrition, see the OI Foundation fact sheet titled "Nutrition."

Prognosis

The prognosis for an individual with OI varies greatly depending on the number and severity of symptoms. Despite numerous fractures, restricted activity, and short stature, most adults and children with OI lead productive and successful lives.

Resource

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